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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,033	01/20/2004	D. Wade Walke	LEX-0469-USA	1190

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EXAMINER	
BALLARD, KIMBERLY A	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 09/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/761,033	WALKE ET AL.	
	Examiner	Art Unit	
	Kimberly A. Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 5-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/20/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The preliminary amendment filed January 20, 2004 has been entered. Claims 2-4 have been canceled and new claims 6-8 have been added. Accordingly, claims 1 and 5-8 are pending and under examination in the instant office action.

Specification

The disclosure is objected to because of the following informalities: on page 1 of the specification, the current status of the parent application, US Application No. 09/875,811, needs to be updated to reflect its issuance as US Patent No. 6,703,495.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 5-8 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility.

The claims are drawn to an isolated nucleic acid molecule comprising SEQ ID NOS: 1, 3, 5, 7 or 11, and recombinant expression vectors and host cells comprising said nucleic acid.

The specification asserts that the invention has utility in that "[t]he *novel* human proteins (NHPS) *described for the first time* herein share structural similarity with mammalian ion transporters, sulfate transporters, and particularly the sulfate transporter that has been *associated* with diastrophic dysplasia" [emphasis added], and that "[t]ransporter proteins are integral membrane proteins that mediate or facilitate the passage of materials across the lipid bilayer...[and therefore]...are good drug targets" (pp. 1-2). For example, the specification asserts the disclosed polynucleotide and polypeptide sequences "can be used to identify mutations associated with a particular disease and also as a diagnostic or prognostic assay" (p. 8, lines 11-13). Further, the specification asserts that probes consisting of NHP sequences can be used to screen libraries, assess gene expression patterns (e.g., microarrays), and for drug discovery. The specification also asserts that the NHP products, i.e., NHP proteins, peptides, antibodies, NHP nucleotide sequences, agonists or antagonists, may be used therapeutically in the treatment and diseases or disorders (p. 15).

The assertion that the disclosed NHP nucleotide sequences can be used in the diagnosis and/or treatment of generic diseases or disorders based on their sequence similarity to known sulfate transporter proteins *associated* with diastrophic dysplasia cannot be accepted in the absence of supporting evidence. In contrast to Applicant's assertions, not a single specific assayable function related to a specific transporter molecule or modulation by a specific drug is disclosed for the polynucleotides of SEQ ID NOS: 1, 3, 5, 7 or 11. Further, not a single specific disease state that putatively can be treated by using these NHPs is disclosed. Moreover, because many polynucleotides

may be useful as hybridization probes for screening libraries or for RFLP analysis, and because many genes are putatively important in diagnosis, drug screening, the treatment of diseases and disorders, etc., unless some association with a specific disease or "biological disorder[s] or imbalance[s]" (p. 3), etc. was known in the art, no specific utility exists. One cannot, therefore, reasonably extrapolate what constitutes a specific utility for the polynucleotides of SEQ ID NOS: 1, 3, 5, 7 and 11 because the specific biological activity for these polynucleotides is not known in the art nor specifically described within the instant specification.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (*Trends in Biotech.* 2000; 18: 34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (*Genome Res.* 2000; 10: 398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (*Trends in Genetics*, 1998; 14: 248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi-functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality, because structural similarity often does not necessarily coincide with functional similarity. Finally, Bork et al. (*Trends in Genetics*, 1996; 12: 425-427) add that the

software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence databases and are then considered facts.

Therefore, without knowing the specific function of any of the proteins encoded by the claimed NHP nucleic acid sequences, it is not possible to determine if the sequences or their related products are definitively involved in a specific disease, much less any generically stated disease. As indicated above, the function of the novel NHP sequences cannot be predicted based solely on structural similarity to a protein found in the sequence databases. A good example of mistaken functional identity is noted with the related protein pendrin. Scott et al. (*Nat Genetics*, 1999; 21: 440-443) note that because of its overall homology to known sulfate transporters, when first discovered, pendrin was also assumed to be a sulfate transporter. However, subsequent functional studies by Scott et al. failed to detect evidence of sulfate transport by pendrin, and instead revealed that pendrin functions as a transporter of chloride and iodide. Moreover, even assuming *arguendo* that the claimed NHP nucleic acid sequences indeed encode sulfate transporters based on structural similarity to known sulfate transporters, the relevant art acknowledges that the involvement of the known sulfate transporters in specific diseases is unknown. For example, a sequence search revealed that that amino acids 1-646 of the NHP sequence encoded by SEQ ID NO: 1, for example, are 100% identical to those of the anion exchanger SLC26A7 disclosed by Lohi et al. (*J Biol Chem*, 2002; 277(16): 14246-14254), and therefore the polypeptide

of SEQ ID NO: 2 (which is encoded by the nucleic acid sequence of SEQ ID NO: 1), for example, is substantially homologous to SLC26A7. However, Lohi et al. note that there is no known connection between SLC26A7 and a disease or disease state (see, for example, Table 1, p. 14247). Additionally, when expressed in *Xenopus* oocytes for functional analysis, the SLC26A7 protein appears to mainly be involved in the transport of *chloride* ions, with transport of oxalate and sulfate to a far lesser extent, particularly when compared to related proteins SLC26A8 and SLC26A9 (see p. 14252, Figure 4).

Therefore, based on the discussions above concerning the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the assertion that the claimed nucleotide sequences of SEQ ID NOS: 1, 3, 5, 7 and 11 can be useful for the detection and treatment of recessive autosomal diseases associated with similarly-structured sulfate transporters, cannot be accepted as specific or substantial, and hence both the NHP nucleotide sequences and their encoded amino acid sequences have no patentable utility.

Because no specific utility is described or known for the human NHP sequences of SEQ ID NOS: 1, 3, 5, 7 and 11, and because the specification merely and generically states that NHPs may be useful for the identification of "mutations associated with a particular disease" (p. 8), or may be useful therapeutically either to "directly treat diseases or disorders" (p. 15) or for screening for compounds which can be used "for the treatment of any of a wide variety of symptoms associated with biological disorders or imbalances" (p. 3), the instant invention also lacks a substantial utility. The specification does not establish a clear nexus between any particular disease state and

an altered level or form of the claimed nucleic acid sequences or their encoded amino acid sequences. There is little doubt that, after complete characterization, these sequences may be found to have a specific and substantial utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" use for the claimed invention. Accordingly, the assertion that NHPs can be used diagnostically or therapeutically in the treatment of diseases or disorders is neither substantial nor specific because significant further research would be required before such NHPs could be used in a "real-world" treatment or diagnosis of a disease.

If Applicant can submit evidence (in the form of a declaration under 37 CFR 1.132 or post-filing date publications) supporting the specification's assertion that the nucleotides of SEQ ID NOS: 1, 3, 5, 7 or 11 or their encoded polypeptides have a specific function similar to a known sulfate transporter protein or are specifically involved in a known disease state, wherein the specific function or disease was predicted by the specification as originally filed, such would be viewed favorably as evidence of patentable use.

The claimed invention also lacks a well-established utility. A well-established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. In view of the evidence in the art that structural similarity between polypeptides cannot accurately predict functional similarity, there is no well-established utility for the

sequences of SEQ ID NOS: 1, 3, 5, 7 or 11. In general, there are no well-established utilities for newly discovered biological molecules.

Since the instant specification does not disclose a specific or substantial utility or a well-established utility for the human NHP sequences of SEQ ID NOS: 1, 3, 5, 7 or 11, then the claimed invention drawn to isolated nucleic acid sequences is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 5-8 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on M-F 9AM - 5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kimberly Ballard, Ph.D.
September 8, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER